herewith. The Commissioner is authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-2319 (Our Order No. A-70025/RFT/RMK/NBC).

AMENDMENT

In The Claims

Please add the following new claim 25:

25. The method of claims 1, 7, or 22 wherein said contacted metanephric tissue develops into a functional chimeric kidney in said recipient and wherein the glomeruli of said functional chimeric kidney are vascularized primarily by said recipient and are able to filter plasma.

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REMARKS

New claim 25 has been added which recites metanephric tissue which develops into functional chimeric kidney in a recipient wherein the glomeruli of the functional chimeric kidney are vascularized primarily by the recipient and are capable of filtering plasma. Support for new claim 25 is found on page 4, lines 14-17, page 9, lines 16-18, page 10, lines 11-24, page 12, lines 14-22, page 14, lines 28-31, page 19, lines 1-12 and 13-29, page 21, lines 24-28, and page 22, lines 3-15. *See also* Rogers, *et al., Am J Physiol Regul Integr Comp Physiol.* 280(6):R1865-9 (2001) (showing that rat

metanephroi transplanted into a mouse host develop glomeruli which are vascularized at least in part by host vessels).

Claim Rejections - 35 U.S.C. §103(a) (*Hammerman et al.* in view of *Liu et al*)

Claims 1 (and claims 4 –5 , 17, and 20 which depend therefrom), 7 (and claims 17 and 20 which depend therefrom) , and 22 (and claims 8, 9, 23 and 24 which depend therefrom) stand rejected under 35 U.S.C. §103(a) as being unpatentable under *Hammerman* in view of *Liu.*

The Examiner alleges that *Hammerman* teaches a method of increasing the nephron mass of a mammalian recipient comprising implanting at least one whole metanephros of an embryonic mammalian donor next to the recipient's omentum. The Examiner further argues that although *Hammerman* does not teach the administration of one or more growth factors, *Liu* teaches the enlargement of metanephroi induced by the administration of IGF-I growth factor. The Examiner concludes that it would be obvious for the skilled artisan to contact metanephric tissue with IGF-I growth factor either *in vitro* (claim 1), at the time a ureteroureterostomy is performed (claim 7), or at the time of or after transplant (claim 22), based on the cited references.

Applicant respectfully traverses the rejection.

Applicant notes that the subject matter of *Hammerman* is disqualified as prior art against the claimed invention since the subject matter of *Hammerman* (U.S. Patent Number 5,976,524) and the claimed invention were, at the time the invention was made, subject to an obligation of assignment to the same person under MPEP §706.02 (l)(1). Assignment to Washington University of U.S. Patent Application Serial No. 09/797,201,

filed February 11, 1997, and which issued November 2, 1999 as U.S. Patent No.: 5,976,524 is recorded in the United States Patent and Trademark Office at Reel/Frame 8497/0702. This U.S. Patent Application Serial No. 09/222,460, filed December 29, 1998, was assigned to Washington University and is recorded in the United States Patent and Trademark Office at Reel/Frame 9910/0171.

This application is a Continued Prosecution Application under 37 CFR §1.53(d). Accordingly, Applicant is entitled to a new filing date and eligible to receive the benefit of MPEP §706.02 (l)(1) (*e.g.*, effective November 29, 1999) for disqualifying *Hammerman* as a prior art reference against the claimed invention.

Since *Hammerman* is the primary reference under all pending 35 U.S.C. §103(a) rejections and is disqualified as prior art against the claimed invention pursuant to MPEP §706.02 (l)(1), it is submitted that the secondary references do not render the claims unpatentable. *Liu* teaches the exogenous administration of IGF-1 to mouse metanephroi stored in organ culture, wherein addition of IGF-I growth factor is correlated with metanephric enlargement and the synthesis of extracellular matrix proteoglycans. As distinguished from Applicant's claims, *Liu* fails to either teach or disclose the contacting of metanephric tissue with one or more growth factors wherein the metanephric tissue is transplanted into a recipient (as required by claim 1), the contacting of metanephric tissue with one or more growth factors in a recipient either at the time of ureteroureterostomy (as required by amended claim 7) or, the contacting of metanephric tissue in a recipient *in vivo* at the time of or after transplant (as required by amended claim 22).

For the foregoing reasons, Applicant respectfully requests reconsideration and withdrawal of the outstanding rejection of claim 1 (and claims 4 –5 , 17, and 20 which

depend therefrom), claim 7 (and claims 17 and 20 which depend therefrom), and claim 22 (and claims 8, 9, 23 and 24 which depend therefrom).

Claim Rejections - 35 U.S.C. §103(a) (*Hammerman et al.* in view of *Rogers et al*)

Claims 1 (and claims 4 –5 , 17, and 20 which depend therefrom), 7 (and claims 17 and 20 which depend therefrom), and 22 (and claims 8, 9, 23 and 24 which depend therefrom) stand rejected under 35 U.S.C. §103(a) as being unpatentable under *Hammerman* in view of *Rogers.*

The Examiner argues that Applicant's invention would be obvious to the ordinarily skilled artisan in light of *Hammerman* in view of *Rogers*. More specifically, the Examiner alleges that *Hammerman* teaches implantation of metanephroi, while *Rogers* teaches contact with TGF-α growth factor for increasing metanephroi size and morphology. The Examiner concludes that it would have been obvious for the skilled artisan to administer exogenous TGF-α subsequent to transplantation for inducing the growth and differentiation of metanephroi.

Applicant respectfully traverses the rejection.

Applicant reiterates that *Hammerman* is disqualified as prior art against the claimed invention pursuant to MPEP §706.02 (l)(1) and *Rogers* is a secondary reference which does not render the claims unpatenable.

The TGF-α growth factor disclosed in *Rogers* is endogenously produced by metanephroi which are grown in a chemically defined organ culture. Applicant's claims are distinguished from *Rogers* in that Applicant teaches treatment of metanephric tissue

with a solution containing one or more exogenously administered growth factors which are specifically demonstrated to induce metanephric tissue development. The growth factors recited in claims 1, 7, and 22 are exogenously administered, rather than endogenously produced.

Accordingly, *Rogers* does not teach or suggest every limitation of the claims. The Examiner has thus failed to establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a) and Applicant requests reconsideration and withdrawal of the outstanding rejections of claims 1 (and claims 4 –5 , 17, and 20 which depend therefrom), 7 (and claims 17 and 20 which depend therefrom), and 22 (and claims 8, 9, 23 and 24 which depend therefrom).

Based on the foregoing, it is submitted that claims 1, 7, 4, 5, 8-9,17, 20 and 22-24 are patentable over the art of record.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance. If upon, upon review, the Examiner feels there are additional outstanding issues, the Examiner is invited to direct any calls in connection with this application to the undersigned at (415) 781-1989.

Dated: Oct 23, 2002

Respectfully submitted,

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VERSIONS WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

25. (New) The method of claims 1, 7, or 22 wherein said contacted metanephric tissue develops into a functional chimeric kidney in said recipient and wherein the glomeruli of said functional chimeric kidney are vascularized primarily by said recipient and are able to filter plasma.

Pending Claims 1, 4, 5, 7-9, 17, 20 and 22-25

1. A method for the treatment of metanephric tissue for transplantation into a recipient comprising contacting said metanephric tissue, *in vitro*, with a growth factor-containing composition comprising one or more growth factors for metanephric development and transplanting said metanephric tissue into said recipient.

4. The method of claim 1 wherein said metanephric tissue is contacted with said growth factor-containing composition for less than 8 hours.

5. The method of claim 1 wherein said metanephric tissue is contacted with said growth factor-containing composition for less than 2 hours.

7. A method for the treatment of metanephric tissue transplanted into a recipient comprising contacting said transplanted metanephric tissue with a growth factor-containing composition comprising one or more growth factors for metanephric development, wherein said growth factor-containing composition is administered to said transplanted metanephric tissue at the time a ureteroureterostomy is performed.

8. The method of claim 22 wherein said growth factor-containing composition is administered to said metanephric tissue by an osmotic pump.

9. The method of claim 22 wherein said growth factor-containing composition is administered to said recipient in a manner such that said one or more growth factors for metanephric development are present in said recipient's blood that circulates through said metanephric tissue.

17. The method of claim 1 or 7 wherein said growth factor-containing composition comprises vascular endothelial growth factor.

20. The method of claim 1 or 7 wherein said growth factor-containing composition comprises vitamin A.

22. A method for the treatment of metanephric tissue comprising contacting said metanephric tissue, *in vivo*, with a growth factor-containing composition comprising one or more growth factors for metanephric development at the time of or after being transplanted into said recipient.

23. The method of claim 22 wherein said growth factor-containing composition comprises vascular endothelial growth factor.

24. The method of claim 22 wherein said growth factor-containing composition comprises vitamin A.

25. (New) The method of claims 1, 7, or 22 wherein said contacted metanephric tissue develops into a functional chimeric kidney in said recipient and wherein the glomeruli of said functional chimeric kidney are vascularized primarily by said recipient and are able to filter plasma.